Remarks/Arguments

Claim 25 was rejected under 35 USC 103(a) over Remiszewski et al in view of Verner et al and Griffin et al. Applicants request reconsideration and withdrawal of this rejection for the reasons that follow.

The present claims relate the treatment of AML with the combination of the FLT-3 inhibitor midostaurin (PKC412) and an HDAI selected from two structurally related compounds: N-hydroxy-3-[4-[[(2-hydroxyethyl)[2-(1H-indol-3-yl)ethyl]-amino]methyl]phenyl]-2E-2-propenamide (LAQ824), and *N*-hydroxy-3-[4-[[[2-(2-methyl-1*H*-indol-3-yl)-ethyl]-amino]methyl]phenyl]-2*E*-2-propenamide (LBH589).

In the Office action, the Examiner sets forth the reasons for asserting that the presently claimed invention is *prima facie* obvious over the cited references. However, the Examiner does not provide any reason for maintaining the rejections in view of the rebuttal evidence provided in the present specification and in the journal article: Bali et al, *Clinical Cancer Research*, **Vol. 10**, 4991-4997, August 1, 2004 ("Bali et al"), which is of record in this application. Applicants have previously argued that this rebuttal evidence demonstrates the patentability of the present invention.

Applicants assert that the present invention is not *prima facie* obvious over the cited references. Although the prior art discloses that HDAIs and FLT-3 kinase inhibitors have utility in some of the same conditions and that HDAIs may be combined with other therapeutic agents, nothing in the combined disclosure of the references would lead the skilled artisan to expect that any benefit would be achieved in AML by combining midostaurin with the present HDAI. Therefore, the present claims are not *prima facie* obvious over the combined disclosure of the references.

Even if the presently claimed invention is prima facie obvious over the combination of references, Bali et al and the present specification provide rebuttal evidence. Applicants assert that the skilled artisan would not have a reasonable basis to expect that such experiments would demonstrate that the combination of a FLT-3 inhibitor and an HDAI to induce apoptosis of MV4-22 cells synergistically and induce more apoptosis of the primary AML cells expressing mutant FLT-3, as demonstrated by the data that is of record. Therefore, the presently claimed invention is patentable over the references.

Applicants further direct the Examiner's attention to the disclosure at page 53-55 of the specification, which describes experiments similar or identical to those described in Bali et al.

Applicants assert that nothing in the combined disclosure of the references would lead the skilled artisan to expect the results demonstrated in Bali et al and the present examples. Therefore, the present claims are patentable over the combined disclosure of the references.

Applicants request withdrawal of the rejection under 35 USC 103(a) for the reasons discussed above.

Entry of this amendment and reconsideration and allowance of the claims are respectfully requested.

Respectfully submitted,

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